mivacurium may be acceptable. Neither drug can be considered a full replacement for succinylcholine, however.

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Preparing Children for Anesthesia and Surgery

IN PREPARING A CHILD for surgery, an anesthesiologist is faced with the unenviable task of separating a starved and frightened child from anxious parents. The scientific rationale for a lengthy preoperative fast has recently been questioned, and based on new studies, preoperative fasting guidelines have been modified. In addition, newer hypnotic drugs and modes of administration can ease the separation of children from their parents.

Whereas the tradition of a preoperative fast can be traced to 1858, decades of studying the epidemiology and risk factors for perianesthetic aspiration of stomach contents have not determined the proper duration of the fast. It has now been established that the gastric fluid of children (older than 1 year) who are allowed to drink clear liquids up until two hours before anesthesia is no greater in acidity or volume than that of children who fast overnight. Therefore, ingesting clear liquids up to two hours before an operation does not appear to increase anesthetic risk. Because substantial physiologic benefit from a shortened fast has not yet been demonstrated, children with esophageal or gastric disease, severe neurologic disease, suffering from pain, receiving narcotics, or presenting airway management difficulties would be likely to benefit from more conservative fasting guidelines. In addition, until more data become available, infants younger than 1 year should fast for three to four hours before a surgical procedure.

The "shot to calm you" is understandably unpopular with children and parents alike. Oral, rectal, or nasal administration of the water-soluble benzodiazepine midazolam hydrochloride is an effective and painless alternative to intramuscular administration. Sedative doses of midazolam when given by these routes range between 0.5 and 1.0 mg per kg. About half of the drug is bioavailable following oral or rectal administration, and the maximal sedative effect will occur within 20 to 30 minutes. Administering the drug nasally increases bioavailability (to about 75%) and provides an even more rapid onset. Because the effects generally dissipate within an hour, recovery from anesthesia is not appreciably prolonged. Oral ketamine hydrochloride, 5 to 10 mg per kg, can be substituted for midazolam; some children may experience unpleasant psychomimetic effects, however, and recovery may be prolonged.

An oral transmucosal form of fentanyl citrate (Oralet) is now available. This consists of a medicated lozenge on a plastic holder. The dose of fentanyl (200 to 400 μg) in each Oralet is substantial, mandating strict adherence to administration and monitoring precautions.

In recent years the preoperative preparation of children for anesthesia and surgery has been reevaluated. Less stringent preoperative fasting guidelines and improvements in preoperative medication techniques have resulted in a less traumatic anesthetic experience without compromising safety.

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Inhaled Nitric Oxide

TREATMENT OF pulmonary hypertension with intravenous vasodilators is limited by systemic hypotension (due to the systemic vasodilator effects of all pulmonary vasodilators) and hypoxemia (due to the reversal of hypoxic pulmonary vasoconstriction). Inhaled nitric oxide (NO) now appears to be a major advance in the therapy for pulmonary hypertension.

Vascular endothelium is able to modulate vascular tone by producing substances that dilate the adjacent smooth muscle. In 1987 NO was identified as endothelium-derived relaxing factor. Nitric oxide produced by the endothelium diffuses into vascular smooth muscle, where it activates soluble guanylate cyclase; the subsequent increase in levels of intracellular cyclic guanine monophosphate produces smooth muscle vasodilation. Endothelium-independent nitrovasodilators such as nitroglycerin and sodium nitroprusside also activate guanylate cyclase, but do so by directly releasing NO. They release NO into both the pulmonary and systemic circulations, so that systemic vasodilation accompanies the pulmonary vasodilation. Nitric oxide itself is rapidly inactivated by hemoglobin in blood, so that the effect of inhaled NO may be localized to the lungs. Thus, inhaled NO diffuses from the alveoli to pulmonary vascular muscle and produces pulmonary vasodilation but no systemic effects. Although NO as a component of air pollution has been considered a toxic gas, it has relatively low toxicity; nitrogen oxides such as nitrogen dioxide that form from NO over time are polluting toxic compounds.

In animals, inhaled NO (5 to 80 parts per million) reverses pulmonary hypertension produced by global hypoxia, thromboxane-mimetic infusion, or heparin-protamine interactions. The pulmonary vasodilation is rapid, completely reversible, and selective, with no

systemic vasodilation or other adverse effects. Studies in human volunteers have shown that inhaled NO reversed pulmonary hypertension caused by breathing a hypoxic gas mixture (12% oxygen). The effects of inhaled NO occurred within the first minute of inhalation, and there were no systemic effects.

Inhaled NO (40 ppm) has now been shown to be an effective, selective pulmonary vasodilator in the treatment of acute pulmonary hypertension. In contrast, epoprostenol (formerly prostacyclin) produces dose-related reductions in both pulmonary and systemic vascular resistance. The effects of inhaled NO are fully reversible within five minutes of discontinuation and can be reproduced with repeated administration. Inhaled NO has selectively decreased pulmonary arterial pressure and pulmonary vascular resistance in patients with congenital heart disease and after cardiac surgery. Inhaled NO improves oxygenation in newborns with persistent pulmonary hypertension, presumably by decreasing shunting across a patent foramen ovale or ductus arteriosus.

Inhaled NO has now become a therapeutic option in patients with severe adult respiratory distress syndrome (ARDS). Pulmonary hypertension and hypoxemia universally occur in patients with ARDS; the severity of each relates to mortality. Intravenous pulmonary vasodilator therapy with agents such as nitroglycerin sodium, nitroprusside, alprostadil (prostaglandin E), epoprostenol, and nifedipine results in small decreases in pulmonary arterial pressure but large decreases in systemic blood pressure and arterial oxygenation. The adverse effects on oxygenation occur because the decrease in pulmonary vascular resistance is primarily due to the reversal of hypoxic pulmonary vasoconstriction. In patients with ARDS, inhaled NO can decrease pulmonary vascular resistance and improve oxygenation. The improvement in oxygenation occurs because inhaled NO (as opposed to intravenous vasodilators) is distributed according to ventilation so that the associated vasodilation increases blood flow to well-ventilated alveoli. The magnitude of improvement in pulmonary hypertension and oxygenation is directly related to the degree of abnormality in each. Nitric oxide concentrations of 0.3 to 4.0 ppm are effective, and beneficial effects are sustained during administration periods as long as two months for patients on ventilators.

Although inhaled NO is clearly effective in improving pulmonary hemodynamics and oxygenation, the role of inhaled NO in patients with ARDS requires additional study. By ameliorating pulmonary hypertension and hypoxemia, inhaled NO may decrease the incidence of pulmonary edema, oxygen toxicity, and pulmonary barotrauma, thereby allowing the lungs to heal. The effects of nitric oxide and nitrogen dioxide on repair or fibrosis in injured lungs and on pulmonary host defenses are largely unknown, however. Survival with prolonged administration of inhaled NO was 86% in one major study, but only 14% in another major study. Inhaled NO is currently used by many centers on a "compassionate use" basis for patients with severe hypoxemia, but controlled clinical trials are needed to determine its value in most patients with ARDS.

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Operative Hysteroscopy Intravascular Absorption Syndrome

ANESTHESIOLOGISTS ROUTINELY anticipate, recognize, and treat volume and electrolyte disturbances during transurethral resection of the prostate (TURP syndrome), but it is now established that operative hysteroscopy has the same potential for these serious pathophysiologic changes. The absorbed volume of fluids employed for uterine distention depends on the extent of intrauterine transection of vascular beds, the intrauterine distention pressures, the volume of media used, and the duration of the procedure. The biochemical composition of the instilled fluids determines the physiologic alterations.

Menstruant women have been shown to be at high risk for death or brain damage from even modest hyponatremia and, perhaps even more important, hypoosmolemia. The earliest signs of this syndrome are confusion and bradycardia with systolic and diastolic hypertension. As with the TURP syndrome, it may be advantageous to use regional anesthesia because awake patients are likely to display precursor symptoms that portend impending brain or cardiac dysfunction and injury. For patients subjected to general anesthesia, delayed diagnosis of the syndrome of operative hysteroscopy intravascular absorption (OHIA) can be mitigated against by adhering to a predetermined schedule for sampling patient blood for rapidly measuring the serum sodium concentration. An instillate solution that contains ethanol 1% as a biologic marker can be used to estimate fluid absorption by measuring the end-tidal ethanol content.

Dextran 70 32% in a 10% solution of glucose (Hyskon) is a hyperosmolar, viscous fluid (molecular weight 70,000) that is immiscible in blood and slowly metabolized over several days. It increases plasma oncotic pressure to the extent that it expands blood volume by ten times its absorbed volume. When substantial volumes (> 500 ml) are absorbed, hypervolemic pulmonary edema is to be expected; serum osmolarity and sodium changes are less prominent. Therefore, the use of Hyskon demands meticulous measurement of the instilled volume and a preoperative agreement with the surgeon as to the maximal acceptable volume instilled before the hysteroscopy is stopped. A prominent sign of intravascular overload is decreasing arterial oxygen saturation. Moreover, intravas-